AMENDMENTS TO THE CLAIMS

Please amend the claims without prejudice, without admission, without surrender of subject matter, and without any intention of creating any estoppel as to equivalents, as follows.

1-24. (Cancelled)

25. (Currently Amended) ~~An infectivity-enhanced conditionally replicative adenovirus having (a) a modified fiber protein containing a ligand, by the conditionally replicative adenovirus containing and expressing a nucleotide sequence encoding the ligand, and wherein the ligand comprises Arg-Gly-Asp in the HI loop of the fiber; or the modified conditionally replicative adenovirus containing a fiber knob domain from a different subtype of adenovirus; whereby the ligand or fiber knob domain provides a pathway to cell binding by the modified conditionally replicative adenovirus other than the coxsackie-adenovirus receptor, and thereby enhances infectivity of the conditionally replicative adenovirus in tumor cells over that of wild-type adenovirus; further comprising (b) a tumor-specific promoter operably linked to one or more early genes selected from the group consisting of E1, E2 and E4.~~ An infectivity-enhanced conditionally replicative adenovirus comprising:

(a) a modified fiber protein encoded by the genome of the adenovirus, wherein the modified fiber protein is:

i) an adenoviral fiber protein modified by the presence of a ligand comprising Arg-Gly-Asp in the HI loop of the fiber protein; or

ii) an adenoviral fiber protein modified by replacement of its fiber knob domain with a fiber knob domain from a different subtype of adenovirus;

whereby the ligand or fiber knob domain provides a pathway to cell binding by the modified conditionally replicative adenovirus other than the coxsackie-adenovirus receptor, and thereby enhances infectivity of the conditionally replicative adenovirus in tumor cells over that of wild-type adenovirus; and

(b) a tumor-specific promoter driving the transcription of a gene encoding a protein selected from the group consisting of prostate specific antigen, carcinoembryonic antigen, secretory leukoprotease inhibitor, alpha-fetoprotein, vascular endothelial growth factor, CXCR4 or survivin, wherein one or more early genes selected from the group consisting of E1, E2 and E4 are operably linked to said promoter.

26. (Cancelled)

27. (Previously presented) The infectivity-enhanced conditionally replicative adenovirus of claim 25, wherein the modified conditionally replicative adenovirus has the modified fiber protein containing the ligand comprising Arg-Gly-Asp in the HI loop.

28. (Currently Amended) The infectivity-enhanced conditionally replicative adenovirus of claim25, wherein the modified conditionally replicative adenovirus has the fiber knob domain from a different subtype of adenovirus.

29. (Currently Amended) The infectivity-enhanced conditionally replicative adenovirus of claim 28, wherein the modified conditionally replicative adenovirus is ~~a~~ subtype 5 having the fiber knob domain from an adenovirus subtype 3.

30. (Previously presented) The infectivity-enhanced conditionally replicative adenovirus of claim 25 wherein the modified conditionally replicative adenovirus provides a pathway to cell binding by the adenovirus other than the coxsackie-adenovirus receptor by containing a ligand, and the ligand has the sequence of SEQ. ID. NO: 1.

31. (Previously presented) The infectivity-enhanced conditionally replicative adenovirus of claim 25 wherein the modified conditionally replicative adenovirus is additionally modified by containing and expressing an exogenous nucleotide sequence encoding a therapeutic polypeptide.

32. (Previously presented) The infectivity-enhanced conditionally replicative adenovirus of claim 31 wherein said therapeutic gene is a herpes simplex virus thymidine kinase gene.

33. (Cancelled)

34. (Currently Amended) A method of reducing tumor burden in a subject in need thereof comprising administering to the subject a therapeutically effective amount of a modified human conditionally replicative adenovirus subtype 5 (hAd5); ~~said modified conditionally replicative adenovirus~~ having greater infectivity in tumor cells than wild-type adenovirus, ~~and hence is modified, by~~ wherein:

the ~~modified conditionally replicative adenovirus is a subtype 5 containing~~ hAd5 contains and ~~expressing~~ expresses a nucleotide sequence encoding ~~the~~ a fiber knob domain from an adenovirus subtype 3~~; whereby the fiber knob domain provides~~ thereby providing a pathway to cell binding ~~by the modified conditionally replicative adenovirus~~ other than the coxsackie-

adenovirus receptor~~,~~ and ~~thereby enhances~~ enhanced infectivity of the ~~of the~~ conditionally replicative adenovirus in tumor cells over that of wild-type adenovirus,

~~and~~ further wherein the modified conditionally replicative adenovirus contains a deletion of the E1A promoter, ~~nucleotide sequence encoding~~ and insertion of a ~~VEGF~~ promoter region selected from the group consisting of prostate specific antigen, carcinoembryonic antigen, secretory leukoprotease inhibitor, alpha-fetoprotein, vascular endothelial growth factor, CXCR4 or survivin, such that ~~the infectivity enhanced conditionally replicative adenonovirus replicates~~ replication is more ~~efficiently~~ efficient in tumor cells than in most normal cell types.

35. (Previously Presented) The method of claim 34 wherein the modified conditionally replicative adenovirus suppresses tumor growth of non-small cell lung cancer.

36. (Previously Presented) The method of claim 34 wherein the modified conditionally replicative adenovirus suppresses tumor growth of ovarian cancer.

37. (Previously Presented) The method of claim 34 wherein the modified conditionally replicative adenovirus suppresses tumor growth of gastric cancer.

38. (Previously Presented) The method of claim 34 wherein the modified conditionally replicative adenovirus suppresses tumor growth of pancreatic cancer.

39. (Previously Presented) The method of claim 34 wherein the modified conditionally replicative adenovirus does not cause hepatic injury.

40. (Previously Presented) The method of claim 34 wherein the modified conditionally replicative adenovirus is additionally modified by containing and expressing an exogenous nucleotide sequence encoding a therapeutic polypeptide.

41. (Previously Presented) The method of claim 40 wherein said therapeutic gene is a herpes simplex virus thymidine kinase gene

42. (Previously Presented) The method of claim 41 comprising administering to the patient in need thereof an effective amount of the conditionally replicative adenovirus and further comprising administering ganciclovir to the patient.

43. (Currently Amended) A method of reducing tumor burden in a subject in need thereof comprising administering to the subject a therapeutically effective amount of a modified human conditionally replicative adenovirus subtype 5 (hAd5)~~; said modified conditionally replicative adenovirus~~ having greater infectivity in tumor cells than wild-type adenovirus, ~~and hence is modified, by~~ wherein:

the hAd5 ~~containing and expressing~~ contains and expresses a nucleotide sequence encoding the fiber knob domain of the canine adenovirus type 2~~; whereby the fiber knob domain provides~~ thereby providing a pathway to cell binding ~~by the modified conditionally replicative adenovirus~~ other than the coxsackie-adenovirus receptor~~,~~ and ~~thereby enhances~~ enhanced infectivity of the ~~of the~~ conditionally replicative adenovirus in tumor cells over that of wild-type adenovirus,

~~and~~ further wherein the modified conditionally replicative adenovirus contains ~~a nucleotide sequence encoding either CXCR4 or survivin promoters~~ a deletion of the E1A promoter, and insertion of a tumor-specific promoter from a gene encoding a protein selected from the group consisting of prostate specific antigen, carcinoembryonic antigen, secretory leukoprotease inhibitor, alpha-fetoprotein, vascular endothelial growth factor, CXCR4 or survivin, such that ~~the infectivity enhanced conditionally replicative adenonovirus replicates~~ replication is more ~~efficiently~~ efficient in tumor cells than in most normal cell types.

44. (Previously Presented) The method according to claim 43 wherein the modified conditionally replicative adenovirus suppresses tumor growth of human breast cancer.

45. (New) An infectivity-enhanced conditionally replicative adenovirus comprising a fusion protein sCAR-EGF, thereby providing increased targeting of the adenoviral vector to tumor cells over non-tumor cells, further comprising a deletion of the E1A promoter, and insertion of a tumor-specific promoter from a gene encoding a protein selected from the group consisting of prostate specific antigen, carcinoembryonic antigen, secretory leukoprotease inhibitor, alpha-fetoprotein, vascular endothelial growth factor, CXCR4 or survivin, such that ~~the~~ replication is more efficient in tumor cells than in most normal cell types.

46. (New) A method of reducing tumor burden in a subject in need thereof comprising administering to the subject a therapeutically effective amount of the infectivity-enhanced conditionally replicative adenovirus of claim 45.